Remarks/Arguments

Applicants respectfully request favorable reconsideration of the subject application, particularly in view of the above amendment and the following remarks. Applicants respectfully urge that there is no additional fee for this amendment because the number of independent claims and the total number of claims in the application have been reduced.

Before proceeding further, the undersigned wishes to thank Examiners Rosanne Kosson and Francisco Prats for their assistance in developing a potential strategy for responding to the pending Office Action during the course of a telephone interview conducted on 21 October 2004. The guidance they provided is greatly appreciated.

Claims 1-24 are currently pending in the subject application. As a result of a requirement for restriction of the subject application imposed by the Examiner, Claims 1-19 and 22-24 have been canceled from the application.

Applicants have amended Claim 20 to recite the claimed bacterial culture as a --biologically pure-- culture in order to comply with the requirements of 35 U.S.C. 101 regarding the claiming of statutory subject matter. Applicants have further amended Claim 20 by adding a limitation whereby the claimed biochemical pathway comprises an operon that encodes for selective cleavage of both C-N bonds

of carbazole. This amendment is supported, for example, at Page 21, line 16 to Page 22, line 7 of the specification of the subject application where a procedure for the creation of an operon that encodes for the cleavage of both C-N bonds in carbazole is described. This amendment is further supported by Claim 17 of the application as originally filed. Accordingly, Applicants respectfully urge that this amendment is fully supported by the application as originally filed and, thus, incorporates no impermissible new subject matter into the application.

Applicants have amended Claim 21 to be consistent with amended Claim 20. In addition, Applicants have amended Claim 21 by inserting the requisite SEQ ID NOS.

Applicants have added five new dependent claims, Claims 25-31, to the subject application. Claim 25, which depends from Claim 21, adds the limitation that the operon comprises a gene encoding an amidase capable of selective cleavage of the C-N bond of 2-aminobiphenyl-2,3-diol, support for which may be found, for example, at Page 21, line 20 to Page 22, line 7 of the specification of the subject application as originally filed. Claim 26, which also depends from Claim 20, adds the limitation that the operon comprises at least one gene capable of converting carbazole to 2-aminobiphenyl-2,3-diol and at least one additional gene capable of selectively cleaving the C-N bond of 2-aminobiphenyl-2,3-diol. Claim 27, which depends from

Claim 26, adds the limitation that the at least one gene capable of converting carbazole to 2-aminobiphenyl-2,3-diol is a *carA* gene. Claim 28, which depends from Claim 26, adds the limitation that the at least one additional gene recited in Claim 26 encodes an amidase capable of selectively cleaving the C-N bond of 2-aminobiphenyl-2,3-diol. Claim 29, which depends from Claim 28, adds the further limitation that the at least one additional gene capable of selectively cleaving the C-N bond of 2-aminobiphenyl-2,3-diol is an *amdA* gene (SEQ ID NO. 4) from *Rhodococcus erythropolis* MP50. Claim 30, which depends from independent Claim 20, adds the limitation that the operon encodes for selective cleavage of both C-N bonds of carbazole without further degradation of the carbazole. Claim 31, which depends from Claim 30, adds the limitation that the operon comprises active *car* consisting of the *carAa, carAc,* and *carAd* genes and an *amdA* gene (SEQ ID NO. 4) from *Rhodococcus erythropolis* MP50 or a *triA* gene of *Pseudomonas sp.* NRRLB-12227 (GenBank Accession No. AF312304). These additional claims are fully supported, for example, at Page 21, line 20 to Page 23, line 3 of the specification of the subject application as originally filed. Accordingly, Applicants respectfully urge that this amendment is fully supported by the application as originally filed and, thus, incorporates no impermissible new subject matter into the application.

The Examiner has indicated that the Information Disclosure Statement filed June 6, 2003 fails to comply with 37 CFR 1.98(a)(2), which requires that a legible copy of each U.S. and foreign patent; each publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed be provided. The Examiner has indicated that certain references were cited by Applicants without the requisite submission of copies of these references. Applicants respectfully urge that copies of each and every reference cited by Applicants on Form PTO-1449 filed on June 6, 2003 *were provided by Applicants.* In support of this assertion, Applicants are enclosing a copy of the return receipt postcard stamped by the U.S. Patent and Trademark Office mail room evidencing receipt of all items listed thereon, including each and every reference cited on Form PTO-1449. Notwithstanding, Applicants are enclosing another Information Disclosure Statement including copies of the references indicated by the Examiner not to have been received with the Information Disclosure Statement filed on June 6, 2003. As copies of these references were originally filed by Applicants, Applicants respectfully urge that no fee pursuant to 37 CFR 1.97(e) should be required.

Claim 21 has been objected to due to the omission of the SEQ ID NOS for identification of the corresponding sequences in the Sequence Listing. In response to this objection, Applicants have amended Claim 21 to include the requisite SEQ ID

NOS. Accordingly, Applicants respectfully urge that this amendment overcomes this objection.

Claim 20 has been rejected under 35 U.S.C. 101 on the basis that the claimed invention is directed to non-statutory subject matter. In response to this rejection, Applicants have amended the claims to identify the claimed strain as "a biologically pure culture" as suggested by the Examiner. Accordingly, Applicants respectfully urge that this amendment overcomes this rejection.

Claim 21 has been rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The Examiner alleges that the specification of the subject application does not disclose a repeatable process to obtain the claimed microorganism and that it is not apparent that the microorganism is readily available to the public. In response, this will confirm that the microorganism in question, *Sphingomonas sp.* ATCC No. BAA-487, was filed under the terms of the Budapest Treaty with the American Type Culture Collection; that access to the invention will be afforded to the Commissioner upon request during the pendency of this application; that all restrictions upon availability to the public will be irrevocably removed upon granting of the patent; that the deposit will be maintained in a public

depository for a period of 30 years or 5 years after the last request or for the effective life of the patent, whichever is longer; and the deposit will be replaced if it should ever become unviable.

The invention claimed by Applicants is a biologically pure culture comprising a biochemical pathway comprising an operon that encodes for selective cleavage of both C-N bonds of carbazole. As used in the subject application, the term "selective" means that the C-N bonds of carbazole are cleaved while leaving the remaining parts of the molecule intact as discussed, for example, at Page 21, line 16 to Page 22, line 7 of the specification of the subject application. In accordance with one preferred embodiment of this invention, the operon comprises active *car* genes consisting of *carAa* (SEQ ID NO. 1), *carAc* (SEQ ID NO. 2), and *carAd* (SEQ ID NO. 3), which convert the carbazole to 2-aminobiphenyl-2,3-diol and a gene encoding an amidase capable of selective cleavage of the C-N bond of said 2-aminobiphenyl-2,3-diol.. As discussed at Page 22, lines 15-17 of the specification of the subject application, carbazole degradation genes, such as the *carB* gene, present in a bacterial host should be inactivated by deletion or insertion mutagenesis so that degradation of carbazole is no longer possible. For the reasons set forth herein below, Applicants respectfully urge that the prior art relied upon by the Examiner as the basis for

rejection of the subject application neither teaches nor suggests the invention claimed by Applicants.

Claim 20 has been rejected under 35 U.S.C. 102(b) as being anticipated by Sierra, U.S. Patent 3,276,840 (hereinafter "the Sierra patent") or by Sato et al., J. Bacteriology 179 (15):4841-4849, 1997 (hereinafter "the Sato et al. publication") or by Outtrup, U.S. Patent 5,856,167 (hereinafter "the Outtrup '167 patent") or by Outtrup, U.S. Patent 5,888,797 (hereinafter "the Outtrup '797 patent") or by Outtrup, U.S. Patent 5,928,929 (hereinafter "the Outtrup '929 patent"). This rejection is respectfully traversed. The Sierra patent teaches a method for promoting the germination of bacterial spores employing a proteolytic enzyme extracted from bacterial spores of *Bacillus subtilis* and Clostridium genera containing subtilisin, a protease that selectively breaks down protein spores to allow germination and which is known to hydrolyze proteins with broad specificity for peptide bonds. Applicants respectfully urge, however, that the Sierra patent neither teaches nor suggests a biologically pure culture comprising an operon which encodes for selective cleavage of both C-N bonds of carbazole as required by Applicants' claimed invention.

The Outtrup '167 patent teaches a protease obtained from a *Bacillus sp.* culture suitable for breaking down protein residues in laundry. Applicants respectfully urge, however, that the Sierra patent neither teaches nor suggests a

biologically pure culture comprising an operon which encodes for selective cleavage of both C-N bonds of carbazole as required by Applicants' claimed invention.

The Outtrup '797 patent teaches a detergent protease obtainable from a strain of *Bacillus sp.* ZI 315 and a process for the preparation of such protease, the use of the protease as a detergent enzyme, and detergent compositions comprising the protease of the invention. Applicants respectfully urge, however, that the Sierra patent neither teaches nor suggests a biologically pure culture comprising an operon which encodes for selective cleavage of both C-N bonds of carbazole as required by Applicants' claimed invention.

The Outtrup '929 patent teaches a detergent protease obtainable from a strain of *Bacillus sp.* I 612 and a process for the preparation of such protease, the use of the protease as a detergent enzyme, and detergent compositions comprising the protease of the invention. Applicants respectfully urge, however, that the Sierra patent neither teaches nor suggests a biologically pure culture comprising an operon which encodes for selective cleavage of both C-N bonds of carbazole as required by Applicants' claimed invention.

The Sato et al. publication teaches the use of *Pseudomonas* sp. strain CA10 for the degradation of carbazole. The initial step of the degradation is considered to be dioxygenation at the angular position adjacent to the nitrogen atom

to give the dihydroxylated intermediate, which spontaneously converts to 2'-aminobiphenyl-2,3-diol after which extradiol dioxygenase attacks the hydroxylated ring at the *meta* position. Hydrolysis of the *meta*-cleavage compound yields anthranilic acid, which is further converted to catechol, which is considered to be metabolized through the β-ketoadipate pathway (Page 4841, Col. 2). The degradation pathway of carbazole using *Pseudomonas* sp. strain CA10 is shown in Fig. 1. As clearly shown, *only one C-N bond is cleaved* by the *Pseudomonas* sp. strain CA10. After the initial cleavage of the C-N bond, the carbazole compound is degraded employing the *carB* and *carC* genes of the *Pseudomonas* sp. strain CA10, leaving the second C-N bond intact. In contrast thereto, the culture of the invention claimed by Applicants comprises an operon which selectively cleaves both C-N bonds of carbazole. In addition, because in accordance with one embodiment of this invention only active *carA* genes, namely, *carAa, carAc,* and *CarAd*, are present in the operon claimed by Applicants, further degradation of the carbazole molecule after the selective cleavage of both C-N bonds is precluded. Applicants respectfully urge that the Sato et al. publication neither teaches nor suggests a biologically pure culture comprising an operon which encodes for selective cleavage of both C-N bonds of carbazole as required by Applicants' claimed invention. Accordingly, Applicants respectfully urge that the Sierra patent, the Outtrup '167 patent, the Outtrup '797

patent, and the Outtrup '797 patent, none of which teach or suggest a biologically pure culture comprising an operon which encodes for selective cleavage of both C-N bonds of carbazole as claimed by Applicants, anticipate the invention claimed by Applicants in the manner required by 35 U.S.C. 102(b).

Claims 20 and 21 have been rejected under 35 U.S.C. 102(a) as being anticipated by Kilbane et al., Biochem Biophys Res Comm 297(2):242-248 (hereinafter "the Kilbane et al. publication"). This rejection is respectfully traversed. The Examiner asserts that the authors of the cited reference are a different inventive entity than the inventors of the subject application. In response to this rejection, Applicants are enclosing a Declaration by Inventors in which the inventors declare and state that they are the inventors of the invention claimed in the subject application, that the contributions of the non-inventor co-authors of the Kilbane et al. publication were merely in the form of activities carried out under the direction of the inventors, and that the non-inventor co-authors did not contribute to the making of the invention claimed in the subject application. In view of this Declaration by Inventors, Applicants respectfully urge that the Kilbane et al. publication does not anticipate the invention claimed by Applicants in the manner required by 35 U.S.C. 102(a).

Conclusion

Applicants intend to be fully responsive to the outstanding Office Action. If the Examiner detects any issue which the Examiner believes Applicants have not addressed in this response, Applicants urge the Examiner to contact the undersigned.

Applicants sincerely believe that this patent application is now in condition for allowance and, thus, respectfully request early allowance.

Respectfully submitted,

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